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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,898	11/28/2000	Leroy Hood	P-IS 4403	7808

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EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,898	HOOD ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-9,11,13,15,16,65,70-80,90,95-104,138,139,141 and 143-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-9,11,13,15,16,65,70-80,90,95-104,138,139,141 and 143-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/15/2006 has been entered.

Claims 1, 6-9, 11, 13, 15-16, 65, 70-80, 90, 95-104, 138-139, 141, and 143-189 are pending.

Claims 10, 12, 14, 17-64, 66-69, 81-89, 91-94, 105-137, 140, and 142 are cancelled. Claim 143 was withdrawn in the previous office action mailed 11/15/2005 from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention (carrier waves). In view of the interpretation of a computer readable medium to be a carrier wave (*see* the non-statutory subject matter rejection below), claim 143 is hereby rejoined with claim 141. However, the election requirement for other inventions is still maintained.

Election was made without traverse in the response filed 7/3/2003.

Claims 1, 6-9, 11, 13, 15-16, 65, 70-80, 90, 95-104, 138-139, 141, and 143-189 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 6-9, 11, 13, 15, 65, 70-79, 90, 95-103, 141, 143-152, and 154-189 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1 are directed to a method for determining a comparative expression profile comprising steps of creating a multidimensional space, determining multidimensional coordinate points, determining a health-associated reference expression region, comparing coordinate points, and determining whether the coordinate point is within of the health-associated reference region. Claims 65, 90, and 144 further comprise a step of determining expression levels of molecules.

However, not all processes are statutory under 35 U.S.C. 101. *See Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility.* 1300 O.G. 4, on 22 November 2005 (published at the USPTO web site http://www.uspto.gov/web/patents'patog/week47/OG/TOC.htm). To satisfy 101 requirements, the claim must be for a practical application, which can be met if the claimed invention "transforms" an article or physical object to a different state or thing OR the claimed invention otherwise produces a useful, concrete, and tangible result. If claims are directed to abstract ideas (such as mathematical algorithms), natural phenomena, and laws of nature, the claims must be considered as a whole for determining whether an abstract ideas, natural phenomena, or laws of nature has a particular application.

In the instant case, the claimed method does not transform or reduce an article or a physical object (*e.g.*, array signals) to a different stage or thing because the "result" of the method (*i.e.*, a multidimensional coordinate point in multidimensional space) is merely data (expression information) and is not equivalent to physical transformation. The claims do not recite tangible expression (*i.e.*, real-world result) of determining the location of a multidimensional coordinate point in multidimensional space in a form useful to one skilled in the art. Thus, the method does not recite steps of producing something that is concrete, useful, and tangible, and is not statutory.

Claims 141 and 143 are directed to a computer-readable medium or carrier wave comprising instructions for performing the method of claim 1. A carrier wave is not a physical product and is therefore nonstatutory subject matter. The specification does not define a computer readable medium as a physical product, thus a computer readable medium may be a carrier wave, and is not necessarily a physical object. As neither the claimed computer readable medium or carrier wave is necessarily a physical "product," claims 141 and 143 are rejected as not being directed to statutory subject matter.

Answer to arguments

Applicants argue that the invention is statutory because it requires the measurements of physical objects or activities to be transformed outside of the computer into computer data, *i.e.*, the invention falls under the "safe harbor." In response to the argument, it is noted that the "safe harbor" standard is no longer applicable. Applicants are referred to *Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility.* 1300 O.G. 4, on 22

November 2005, promulgating the requirements for satisfying statutory subject matter under 35 U.S.C. 101, as set forth above.

Lack of Utility

Claim 1, 6-9, 11, 13, 15-16, 65, 70-80, 90, 95-104, 138-139, 141, and 143-189 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claim 1 is directed to a method of determining a comparative expression profile in an individual comprising creating a multidimensional space related to expression levels of molecules, determining a multidimensional point for reference and test individuals, determining a health-associated region for the reference individuals, comparing a multidimensional coordinate point of the individual to the health-associated region of the reference population, and determining whether the multidimensional coordinate point of the individual is outside of the health-associated region which indicates a perturbed expression profile. Claims 90 and 144 are directed to a method of diagnosing a health states in an individual comprising similar steps. The specification on pages 1 and 3 discloses that the instant invention is useful for predictive medicine and efficiently diagnosing a disease based on a gene expression pattern in an individual. However the disclosed utility is not applicable to the instant claims. For example, the claimed methods "determine" whether an expression profile of an individual is "perturbed" from the comparison to a profile to the "health-associated" reference population. Neither the specification, not the claims disclose any information about "health-associated" reference individuals and/or what the "health-associated" reference indicates, *e.g.*, reference individuals are healthy, carry disease markers, carry markers specific for a particular stage of a disease, carry markers for specific alleles, carry ancestral markers, *etc.* Determining that an individual has a

"perturbed" profile without knowing what a reference represents does not provide any information about a disease stage or health conditions of the individual, and therefore does not allow one skilled in the art to "effectively diagnose a disease." Thus, the claimed method does not have a "result" which is "of immediate benefit" because one skilled in the art would not know what "perturbed" profile indicates. Consequently, the instant claims do not have substantial utility (a "real world" use) because the methods do not have a stated correlation between, for example, a disease and a determined perturbation and is not particular to a specific health condition. Therefore, determining what a "perturbed" expression profile indicates would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. The instant invention also does not have a specific utility, because absent any disclosure about, for example, a stage of health or disease and/or allelic markers in a affected and unaffected population, and whether the "reference profile" represents a healthy or diseased, or specific subpopulation, *etc.* (*i.e.*, absent some correlation between a specific population and disease to be diagnosed), the asserted utility is not specific. No such information is recited in the instant claims and further research would be required to determine such a correlation. Applicant is reminded that a "use" to perform further research is not a utility under 35 U.S.C. 101.

Claims 138-139, 141, and 143 are directed to a computer system and a computer readable medium performing steps of the instant methods. Because the method does not have a specific, substantial and credible utility for the reasons set forth above, any computer system and/or program implementing such a method also lacks utility. The system and a computer readable medium in this case perform a method which produces no useful result, and one of ordinary skill

in the art would not know for what purpose or to what useful end such a system might be used for, therefore, the invention lacks utility.

For the reasons stated above claims 1, 6-9, 11, 13, 15-16, 65, 70-80, 90, 95-104, 138-139, 141, and 143-189 lacks patentable utility under 35 U.S.C. 101.

Enablement

Claims 1, 6-9, 11, 13, 15-16, 65, 70-80, 90, 95-104, 138-139, 141, and 143-189 are also rejected under 35 U.S.C. 112, *first paragraph*. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentations is "undue." These factors include, but are not limited to:

a) The breadth of the claims;
b) The nature of the invention;
c) The state of the prior art;
d) The level of one of ordinary skill;

e) The level of predictability in the art;
f) The amount of direction provided by the inventor;
g) The existing of working examples; and
h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

Claims 8, 72, and 96 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a) The claims are broad because they are directed to a method of determining a comparative expression profile in an individual, wherein a multidimensional coordinate point represents a generic expression profile of molecules indicating the course of generic disease. The instant specification does not provide specific guidance to practice the invention because it does not disclose how to determine the "course" of a disease from data taken at a single point in time (*i.e.*, a multidimensional coordinate point) and/or how to determine the "course" of a disease merely by identifying that an expression level is "perturbed".

b) The invention is drawn to a method for of determining a comparative expression profile in an individual.

c) Prior art analysis shows that monitoring the "course" of a disease requires, for example, obtaining a response curve, *i.e.*, measuring gene or protein abundance in cells in

response to a treatment (perturbation) over time. *See* Friend, US 6,324,479, col. 3, lines 34-44; col. 10; Levine, US 6,020,135, col. 7-8. The instant specification does not disclose measuring gene expression over a period of time.

f) The specification does not provide guidance how to determine the "course" of a disease from an expression level taken at a single point and an indication that the profile is "perturbed."

g) The specification does not provide working examples and does not teach how to make and use the instant method without monitoring expression levels over time.

h) In order to practice the claimed invention, one skilled in the art must randomly select a point, determine if the expression profile is perturbed, and must guess the progression of a disease without knowing any information with regard to whether expression levels change over time. This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention, the lack of directions presented in the specification, the complex nature of the invention, and the state of the prior art showing that the monitoring the disease progression requires obtaining gene expression over time, the specification fails to teach one skilled in the art how to use the claimed method for determining expression profiles indicating the course of a disease.

Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 72, 74, 78, 96, 98, 102, and 151 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 74 and 98 recite "expression levels are determined by contacting ... specimen with an array and measuring the expression levels." Claims 78 and 102 recite "expression levels are determined by contacting ... specimen with antibody ligands and measuring the expression levels. It is not clear whether applicants intended to further limit the method steps OR the data. If the latter, then it is not clear what further limitation of data used in the claimed method is intended by the methods of measuring the data. If the former, then the claims should be rewritten using active, positive claim language. As the intended limitation is not clear, claims 74, 78, 98 and 102 are indefinite.

Claims 78, 102, and 151 recite the limitation "antibody ligands." It is not clear whether applicants intended an "antibody" *per se*, a ligand for an antibody, *etc*. It is further not clear what an antibody or ligand is directed to or generated "against". As the intended limitation is not clear, claims 78, 102, and 151 are indefinite.

Claims 90 and 144 recite in the preamble "[a] method of diagnosing a health state in an individual." The methods comprise steps of determining a comparative expression profile in an individual comprising creating a multidimensional space related to expression levels of molecules, determining a multidimensional point for reference and test individuals, determining a health-associated region for the reference individuals, comparing a multidimensional coordinate point of the individual to the health-associated region of the reference population, and determining whether the multidimensional coordinate point of the individual is outside of the

health-associated region which indicates a perturbed expression profile. None of the steps is actually directed to "diagnosing a health state in an individual." The "result" of the method is "determining" whether an individual has a "perturbed" profile in comparison to some unidentified "health-associated" reference. It is not clear what further steps are intended for "diagnosing." It is further unclear whether the preamble is intended to limit the method and what relationship is intended between the preamble and the method steps. Thus, claims 90, 95-104, and 144-153 are indefinite.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Le, US 6,153,115 – Although Le discloses a multidimensional analysis similar to that recited in the instant method, the examiner determined that the reference in not an analogous art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marina Miller
Examiner
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MM

MARJORIE A. MORAN
PRIMARY EXAMINER
Marjorie A. Moran
7/17/06